REMARKS

I. Status of the Claims

Claims 1-34 are pending in the application.

Claims 1-4, 8-9 and 16-19 are under consideration in the present patent application and have been examined.

Claims 1-4, 8-9 and 16-19 stand rejected under 35 U.S.C. §101 because the Patent Office contends the claims are not supported by either a credible, specific and substantial asserted utility or a well established utility.

Claims 1-4, 8-9 and 16-19 also stand rejected under 35 U.S.C. §112, first paragraph, because the Patent Office contends one skilled in the art would not know how to use the claimed invention.

Claims 1-4, 8-9 and 16-19 additionally stand rejected under 35 U.S.C. §112, second paragraph, because the Patent Office contends the claims are indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention.

II. Response to the Objections to the Specification

The Patent Office objected to the specification. Specifically, the Patent Office objected to the Abstract because the legal term "said" is used therein. Applicants have amended the Abstract to remove the term "said" and have replaced it with the term "K+betaM3." Accordingly, applicants request that the objection to the Specification be withdrawn.

The Patent Office also objected to the specification because it contains an embedded hyperlink and/or other form of browser-executable code. Applicants have amended the Specification to remove all hyperlinks or other forms of browser-executable code. Accordingly, applicants request that the objection to the Specification be withdrawn.

The Patent Office also objected to the Specification because it contains references to "ATCC Deposit No. Z" which, the Patent Office states, are not clear concise and exact. Applicants have amended Table 1 in the Specification to update the Table with the ATCC Deposit Number. However, applicants direct attention to Table 1 on page 41 of the Specification. The heading in the third column of the Table is "ATCC Deposit No. Z and Date." Applicants also direct attention to page 42, lines 12-14, wherein applicants state "The cDNA Clone ID was deposited on the date and given the corresponding deposit number listed in "ATCC Deposit No:Z and Date." "Vector" refers to the type of vector contained in the cDNA Clone ID."

Thus, instead of listing the data for the ATCC deposit number in the specification, for convenience applicants refer to the deposit number as "ATCC Deposit No. Z", which is presented in Table 1. In view of applicants' presentation of Table 1 on page 41, and its legend on page 42 of the Specification, applicants submit that the references to "ATCC Deposit No. Z" are clear, concise and exact. Accordingly, applicants request that the objection to the Specification be withdrawn.

III. Response to the Rejection of Claims 1-4, 8-9 and 16-19 Under 35 U.S.C. §101

The Patent Office rejected claims 1-4, 6-8 and 16-19 under 35 U.S.C. §101 "because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation." Office Action, page 3. Applicants traverse the rejection and submit the following comments.

It is well established that when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the Examiner unless the Patent Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." Fujikawa v Wattanasin, 93 F.3d 1559, 1565 (Fed. Cir. 1996).

Bearing the above in mind, the Patent Office's rejections under 35 U.S.C. §101 will be addressed individually in the following paragraphs.

III.A. Applicants' Characterization of the Claimed Sequences

The Patent Office first characterizes the claimed sequences by reciting elements of claim 1. The Patent Office then contends the Specification does not disclose any significant or functional characteristics of the claimed sequence. The Patent Office further contends the Specification does not disclose any working examples that are involved in any of the recited activities. The Patent Office concludes the utilities of the sequences are not substantial. Thus, it appears that the Patent Office is asserting the position that applicants have not adequately characterized the claimed sequences. Applicants disagree with the Patent Office's analysis and conclusions in this regard.

Applicants first note that the homology data provided in the specification supports applicants assertion that the claimed sequences are potassium channel beta subunits. Applicants note that the Specification reports homology at the nucleotide and amino acid level between the claimed

sequences and the human Maxi-K potassium channel beta subunit, KCNMB1, the human membrane channel protein-2, the Drosophila CG10465, and the Drosophila CG10440 protein. Applicants direct particular attention to Figures 2 and 4, wherein details regarding the homology between the claimed sequences and other sequences is presented. Applicants specifically note the levels of homology reported, namely 90.7% identity and 92.5% similarity with the human membrane channel protein-2; 32.0% identity and similarity with Human Maxi-K potassium channel beta subunit, 33.1% identity and 42.6% similarity with the Drosophila CG10440 protein; and 24.0% identity and 38.8% similarity with the Drosophila CG10465 protein. Further support for applicants' characterization of the claimed sequences is found in Example 7, wherein RNAi results are presented.

Applicants submit that the above results are presented in a form immediately usable by one of ordinary skill in the art. For example, the implication of the negative role of the claimed sequences in the NF-kB pathway suggests that these sequences could be immediately employed in the design of a therapeutic agent, such as a small molecule modulator or as an antisense or therapeutic RNAi reagent.

Summarily, it is applicants' position that the claimed sequences are characterized to a degree that one of ordinary skill in the art could employ them in any of the applications recited in the Specification, as discussed below.

III.B. Treating, Diagnosing and/or Preventing Diseases, Disorders and Conditions

The Patent Office states applicants' asserted utility of treating, diagnosing and/or preventing numerous diseases, disorders and conditions is not specific or substantial. The Patent Office argues "[t]he specification does not disclose disorders associated with a mutated, deleted, or translocated K+betaM3 gene (SEQ ID NO:1). The specification does not disclose which disorders are associated with altered levels of the K+betaM3 gene." Office Action, page 5. Applicants traverse the rejection and submit the following comments.

Applicants direct attention to page 24, lines 17-20 of the Specification, wherein applicants state: "[b]ased on the expression pattern of this novel sequence, diseases that can be treated with agonists and/or antagonists for K+betaM3 included persistent hyperinsulinemic hypoglycemia of infancy, hyperkalemia and hypokalemia, cystic fibrosis and hypercalciuric nephrolithiasis." Applicants also direct attention to page 29, line 14 to page 35, line 29 of the Specification, wherein Applicants present an extensive discussion of various diseases that can be diagnosed, prognosed, and/or prevented that are related to the expression of the claimed K+betaM3 sequence. The above

specific diseases are only representative, and additional diseases and conditions in which the claimed sequence may play a role are provided in the Specification.

Applicants also direct attention to Example 6 (pages 236-244), wherein the results of antisense experiments are presented. These results provide evidence that the claimed sequence plays a role in the regulation and/or expression of p21. Thus, modulation of the claimed sequence, or the expression of the claimed sequence, can be employed in the treatment of disorders of the mammalian cell cycle. Applicants submit, contrary to the Patent Office's assertions, the specification does, in fact, disclose specific disorders associated with altered levels of the K+betaM3 gene.

Applicants further direct attention to Example 7 (pages 244-249), wherein applicants demonstrate an association of the claimed sequence with the NFκB pathway. This was accomplished by identifying a Drosophila orthologue of the claimed sequence, knocking out the identified orthologue and determining the effect of the knockout using RNAi techniques. The results of these experiments indicate that the Drosophila orthologue is involved in the regulation of the Drosophila innate immune response. Based on the degree of identity/similarity between the Drosophila orthologue and the claimed K+betaM3 sequence, the claimed sequence is likely to have a function is the modulation of one or more mammalian immune pathways. In view of these results, applicants submit, therefore, that the Specification provides yet further specific diseases and conditions (e.g., immune pathway diseases and conditions) associated with altered levels of the claimed sequences.

Applicants also assert that the recited utility is substantial. Applicants submit that this asserted utility is presented in a form in which it can be employed in a real-world sense. The Specification provides guidance in this regard by indicating various conditions in which modulation of the expression of the claimed sequence can be employed to diagnose, prognose and/or prevent, as well as guidance in how to achieve the desired results such as that provided in Examples 24 and 25, for example.

Applicants also disagree with the Patent Office's conclusion that significant experimentation would be required to identify individuals with such a disease. Applicants submit that any such experimentation, if in fact any experimentation would be required, would be simply routine and is unnecessary to identify or confirm a "real world" context. Applicants submit that a "real world" context is already established and no further experimentation is required in this regard.

III.C. Hybridization Probes

The Patent Office argues that applicants' asserted utility of hybridization probes is not substantial or specific. The Patent Office states "[h]ybridization probes can be designed from any polynucleotide sequence Further the specification does not disclose specific cDNA, DNA or RNA targets." Office Action, page 5. Applicants disagree with the Patent Office's analysis. Accordingly, applicants traverse and submit the following remarks.

The Specification provides guidance in the design of nucleic acid hybridization probes that will detect nucleic acid sequences comprising the claimed sequence and/or the cDNA contained in the deposited clone (ATCC Deposit No. PTA-4055). The specification also provides that such probes can hybridize with nucleic acid molecules in biological samples and can be employed in a range of forensic and diagnostic methods. For instance the hybridization probes of the present invention can be employed as reagents in the detection and isolation of a claimed K+betaM3 nucleotide sequence from

Applicants again submit that the homology and Drosophila data presented in the Specification support applicants' contention that the claimed sequence is a K+βM3 is a potassiuum channel β subunit polypeptide. As noted herein, the homology data involves polypeptides that are known to be potassium channels. Applicants are of the position that this observation, in conjunction with the Drosophila data, would convince one of ordinary skill in the art of applicants' assertion. Again, as noted herein, applicants have supplied specific diseases in which the claimed sequence can be employed in the cited utility. Consequently, applicants are of the position that the asserted utility is substantial.

Applicants also believe the cited utility is specific since, although all nucleic acids can be used as probes or primers, not all nucleic acids can be used as primers or probes for the claimed sequence. Thus, applicants contend the asserted utility is specific, substantial and credible, thereby meeting the statutory requirement of utility.

III.D. Making a Fusion Protein

It is the Patent Office's position that applicants' asserted utility of making a fusion protein is not substantial or specific. The Patent Office states "the specification discloses nothing specific or substantial for the fusion protein that is produced by this method." Office Action, page 5. Applicants traverse the rejection.

Applicants direct attention to page 71, line 31, through page 72, line 27, wherein applicants describe the formation of a fusion protein that may increase the half-life of the protein in vivo. A

fusion protein of the present invention can also offer advantages in purification, as described in the Specification. A detailed discussion of the advantages, uses and formation of a fusion protein of the present invention is presented starting on page 125, line 12 through page 129, line 6.

The Specification also states various specific uses for the fusion proteins of the present invention. For example, the Specification states "[m]oreover, polypeptides of the present invention may be useful in inhibiting the angiogenesis of proliferative cells or tissues, either alone, as a protein fusion, or in combination with other polypeptides directly or indirectly, as described elsewhere herein" (Specification, page 169, lines 32-35). The Specification further states "Polypeptides, including protein fusions, of the present invention, or fragments thereof may be useful in inhibiting proliferative cells or tissues through the induction of apoptosis." (Page 170, lines 11-13). The Specification also discloses a similar use for fusion proteins of the present invention in inhibiting the metastasis of proliferative cells or tissues (page 170, lines 28-29), and enhancing the immunogenicity and/or antigenicity of proliferating cells or tissues (page 171, lines 12-14). Thus, applicants submit the use of the claimed sequences as fusion proteins provides a specific, substantial and credible utility, and that these fusion proteins can be employed in real world applications, such as those highlighted above.

III.E. Attachment of a K+betaM3 Nucleotide to a Gene Chip

The Patent Office states that the asserted utility of employing a sequence of the present invention as a component of a gene chip is not specific or substantial. The Patent Office sates "the specification does not disclose specific nucleic acid sequences used to generate the gene chip." Office Action, page 6. Applicants traverse the rejection and submit the following comments.

As stated in the specification, "such a gene chip with polynucleotides of the present invention attached may be used to identify polymorphisms between the polynucleotide sequences, with polynucleotides isolated from a test subject. The knowledge of such polymorphisms (i.e. their location, as well as, their existence) would be beneficial in identifying disease loci for many disorders, including proliferative diseases and conditions." (Specification, page 145, lines 27-32).

Applicants submit that the above representative discussion, coupled with applicants arguments in support of the characterization of the claimed sequences as encoding a K+betaM3 potassium channel modulating subunit, supports applicants assertion that the use of the claimed sequences as a component of a gene chip is specific and substantial.

Thus, applicants are of the belief that although a gene chip can be made for any polynucleotide, the present specification discloses particular sequences that can be attached to a gene chip, namely K+betaM3 sequences, and fragments thereof, disclosed. As indicated, such a gene chip could be employed in screening for polymorphisms, for example those associated with a disease state or other undesirable condition. Applicants further submit that the identification of sequences that would be suitable for incorporation into a gene chip is within the skill of one of ordinary skill in the art.

Applicants submit the use of the claimed sequences as an element of a gene chip provides a specific, substantial and credible utility.

III.F. Gene Therapy

The Patent Office states applicants' asserted utility of gene therapy is not specific or substantial. Again, applicants disagree with the Patent Office's characterization of this asserted utility. Accordingly, applicants traverse the rejection.

The Patent Office states "[t]he specification does not disclose diseases associated with a mutated, deleted, or translocated K+betaM3 gene of SEQ ID NO:1. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease." Office Action, page 6. In response, applicants direct attention to the section of the Specification beginning on page 162 and entitled "Biological Activities," and continuing through the sections following the section entitled "Diseases at the Cellular Level" on page 180. In this section, applicants provide both general descriptions of types of diseases and conditions that may be treatable using the polynucleotides of the present invention (e.g., in a gene therapy application) as well as specific diseases and conditions that may be treatable. Support for association of the claimed sequences with these and other conditions is presented in the Examples and Drawings of the instant application. Thus, applicants submit that the specification does in fact describe specific conditions that may be treatable using the polynucleotide sequences of the present invention.

III.G. Construction of a Transgenic Animal

It is the Patent Office's position that applicants' asserted utility of generating a transgeneic animal is not specific or substantial. The Patent Office again contends "[t]he specification does not disclose diseases associated with a mutated, deleted, or translocated K+betaM3 gene of SEQ ID NO:1. Significant further experimentation would be required of the skilled artisan to identify such a

disease." Office Action, page 6. The Patent Office also states there is no disclosure in the Specification regarding "whether the genes will be 'knocked in' or 'knocked out' or what specific tissues and cells are being targeted." Office Action, page 6. Applicants traverse the rejection.

Applicants reiterate their arguments presented herein above regarding the disclosure of the various general and specific disease states and conditions that are related to the sequences claimed in the present application. Summarily, applicants submit that the Specification discloses a range of diseases and conditions that may be treatable by employing (or removing) a polynucleotide sequence of the present invention.

Continuing, applicants direct attention to Example 32, found on page 301 of the Specification. In one aspect, this Example describes incorporating (i.e., "knocking in") a gene (e.g., a gene encoding a K+βM3 polypeptide) into some or all cells of an animal. Continuing, Example 33, found on page 303 of the Specification, describes removing (i.e., "knocking out") a gene (e.g., a gene encoding a K+βM3 polypeptide). The decision to knock in or knock out a gene can depend on the nature of the disease or condition being studied or treated. As discussed in the specification, in some situations it might be desirable to knock in a gene, for example, when expression of the gene is non-existent in the wild type animal. In other situations it might be desirable to knock out a gene, for example when high expression levels of the gene lead to a disease or condition. Examples of both situations are discussed in the Specification.

In view of the above, applicants submit that the generation of a transgenic animal is a substantial, credible and specific utility, since both specific disease states and a discussion of characteristics of the claimed sequence are presented.

III.H. Chromosome Mapping

The Patent Office argues the recited utility of chromosome mapping is not substantial or specific. The Patent Office contends "the specification does not disclose a specific DNA target." Office Action, pages 6-7.

In response, applicants direct attention to Example 14, wherein applicants provide guidance on chromosome mapping. Applicants also provide specific details regarding PCR conditions and types of gels that can be employed. Template DNA can be generated or purchased and can be employed. Using the provided guidance, coupled with knowledge of the claimed sequence as provided in the Specification, applicants submit that one of ordinary skill in the art would not need to employ substantial further research in order to use the sequence as a chromosome map probe.

Applicants submit that one of ordinary skill in the art, employing the guidance provided in the Specification, notably Example 14, would readily be able to use the invention as claimed. Applicants further note that routine experimentation is permissible and, given the guidance provided in the Specification and the high level of skill in the art. Accordingly, applicants submit that the recited utility of chromosome mapping is specific, substantial and credible.

III.I. Tissue Typing

The Patent Office contends the recited utility of tissue typing is not substantial or specific. The Patent Office contends "the specification does not disclose specific DNA sequences for use as markers for RFLP, to prepare primers, or to amplify DNA." Office Action, page 7. Applicants traverse and submit the following comments.

Applicants submit that by providing the claimed sequences and the characterization of the claimed sequences, one of ordinary skill in the art would be able to employ the sequences in the recited utility. Applicants submit that there is no need to recite specific sequences for use as markers or primers. In this regard, applicants note that PCR primers are disclosed in the application, and that such primers were used to amplify DNA. In view of the level of skill in the art and the disclosure of the claimed sequences, applicants submit the recited utility of tissue typing is specific, substantial and credible.

III.J Screening for Therapeutic Compounds

With regard to this recited utility, the Patent Office argues this utility is not specific or substantial because "the specification discloses nothing specific or substantial for the K+betaM3 agonists, antagonists or other agents screened in this method." Office Action, page 7. The Patent Office also argues that "[n]othing is discloses about how the polynucleotide is affected by the compounds." Office Action, page 7. Applicants traverse and submit the following.

Applicants note that the Specification discloses situations (e.g., disease conditions) in which it is desirable that the activity of the claimed sequence is upregulated and other situations in which it is desirable that the activity be downregulated. Modulators can be identified that exhibit either of these properties. Applicants further submit that since applicants are not claiming the modulators, there is no need to provide any detail beyond the fact that such compounds can be identified by screening against the claimed sequences. Applicants note that, although screening assays can be performed with any sequence, but such assays will not identify modulators of the claimed sequence.

Applicants also assert that the recited utility is substantial. According to the Utility Guidelines, an assay method for identifying compounds that themselves have a substantial utility defines a "real world" context of use. Utility Guidelines, page 6. Applicants assert that the compounds identified by the claimed method meet the substantial utility test because they are useful for treating specific disorders,

Applicants submit that in view of the characterization of the claimed sequences and the detail provided in the Specification (see, e.g., page 194, lines 21-33), the use of the claimed sequences in screening operations is a readily applicable in a real world sense. Consequently, applicants submit that this recited utility is specific, substantial and credible.

Summarily, applicants submit that the recited utilities are specific, substantial and credible, and meet the requirement of utility under 35 U.S.C. §101. In this regard, applicants note that only one utility need be disclosed. ("To violate §101 the claimed device must be totally incapable of achieving a useful result." Brooktree Corp. v. Advanced Micro Devices, Inc., 977 F.2d 1555, 1571 (Fed. Cir. 1992)). In the present case, for the reasons presented above, applicants have presented at least one beneficial use for the claimed sequences. Accordingly, applicants request that the rejection of the claims under 35 U.S.C. §101 be reconsidered and withdrawn.

IV. Response to the Rejection of Claims 1-4, 8-9 and 16-19 Under 35 U.S.C. §112, First Paragraph, Utility

The Patent Office rejected claims 1-4, 8-9 and 16-19 under 35 U.S.C. §112, first paragraph, as not supported by a specific and substantial asserted utility or a well established utility. The Patent Office concludes that one skilled in the art would therefore not know how to make and use the claimed invention. Applicants traverse the rejection and submit the following comments.

For the reasons presented herein above, applicants submit that the instant application recites numerous specific, substantial and credible utilities. In addition, applicants note the various examples and discussion presented in the context of each of these recited utilities, including those points in the Specification highlighted above. The Specification provides explicit guidance for these utilities. Given the high level of skill in the art, the guidance provided in the specification and the recitation of several specific, substantial and credible utilities, applicants submit that the disclosure is in full compliance with 35 U.S.C. §112, first paragraph. Accordingly, applicants respectfully

request that the rejection of the claims under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn.

V. Response to the Rejection of Claims 1-4 and 8-9 Under 35 U.S.C. §112, First Paragraph, Enablement

The Patent Office rejected claims 1-4 and 8-9 under 35 U.S.C. §112, first paragraph, failing to comply with the enablement requirement of the statute. The Patent Office based its rejection on its belief that "the specification does not teach any variants, fragments, or allelic variants of the K+betaM3 polynucleotide or polypeptide." Office Action, page 8. The Patent Office continues,

> The specification also does not teach a nucleic acid sequence with 95% sequence identity to the nucleotide sequence of SEQ ID NO:1. The specification does not teach any specific epitopes or domains of the polypeptide encoded by SEQ ID NO:1. Furthermore, regarding allelic variants, it is noted that such are recognized in the art as variant genes which map to the same locus on the chromosome... The specification does not disclose the chromosomal location of any of K+betaM3 gene characterized by the inventors. Additionally, the specification does not teach functional or structural characteristics of any polynucleotide variants in the context of a cell or organism.

Office Action, pages 8-9. Applicants traverse the rejection and submit the following comments.

V.A. Allelic Variants

In response, applicants direct attention to Example 14, wherein applicants provide guidance on chromosome mapping. Applicants submit that one of ordinary skill in the art, employing the guidance provided in the Specification, notably Example 14, would readily be able to use the invention as claimed. Applicants note that routine experimentation is permissible and, given the guidance provided in the Specification and the high level of skill in the art, applicants submit that any experimentation a skilled artisan that might be required to practice the claimed invention would be routine. Applicants are of the position that if any experimentation were to be required, it would not be undue, given the clear guidance provided in the Specification. Applicants further note that guidance is provided in the Specification for performing alignments and other bioinformatic methods which can be employed to identify and/or exploit allelic variants of the claimed sequences.

V.B. Derivatives and Fragments

Continuing, the Patent Office's also rejected the claims under 35 U.S.C. §112, first paragraph, based on applicants' recitation of the use of derivatives and fragments of the claimed sequences. The rejection appears to be based on the Patent Office's position that "applicant has

provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to and the nature and extent of changes that can be made at these positions." Office Action, page 9.

In this regard, it appears that the Patent Office is requiring that applicants submit working examples in order to comply with the requirements of 35 U.S.C. §112, first paragraph. The applicable statute and case law, however, mandates no such requirement. While the presence or absence of working examples can be a consideration in the overall evaluation of enablement, working examples are not required under 35 U.S.C. §112, first paragraph, to comply with the enablement standard presented therein. Indeed, the M.P.E.P. states that a U.S. patent application need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation. M.P.E.P. §2164.02.

Turning next to the Patent Office's assessment of the amount of experimentation required to practice the claimed invention, it is applicants' position that the quantity of experimentation to be performed by one skilled in the art is only one factor involved in determining whether "undue experimentation" is required to make and use the invention. "An extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." In re Colianni, 561 F.2d 220, 224 (C.C.P.A. 1977). "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the U.S. patent application in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed." In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

The specification provides a nucleic acid sequence encoding the claimed K+βM3 polypeptide, as well as the sequence of the encoded polypeptide. Applicants submit that contrary to the Patent Office's position, no experimentation is required, beyond the application of routine molecular biological techniques, in order to use the claimed sequences to make variants and fragments useful for the purposes discussed in the Specification.

As noted above, the polypeptides and polynucleotides of the present invention have been described in the specification. This knowledge can be employed to make, study and use variants of the claimed polypeptides and polynucleotides. Indeed guidance is provided in the specification (see page 50, line 29 through page 67, line 18, including Table 3 presented therein, for example) in preparing such variants. Such variants can be employed in the same roles as the characterized

claimed polypeptides and polynucleotides. For instance, a variant prepared in accordance with the present invention might exhibit an enhanced activity that might be desirable in a given application of the sequences of the present invention.

Applicants again note that the Patent Office's burden is to demonstrate that the disclosure, combined with what is known in the art, does not enable one of ordinary skill in the art to practice the invention commensurate with the scope of the claims. Given the high level of skill in the art, it is applicants' position that the Patent Office has not provided sufficient evidence that one of ordinary skill in the art would not be enabled by the present disclosure, combined with what is known in the art, to employ the compositions and methods of the present disclosure, particularly in view of the specific, substantial and credible utilities recited in the specification and the extensive discussion of derivatives and fragments presented in the Specification.

The Patent Office also rejected the claims because the Patent Office states the Specification does not disclose functional or structural characteristics of any polynucleotide variants in the context of a cell or organism. Applicants submit that there is no requirement that the characteristics that a sequence exhibits in the environment of an organism be disclosed. Applicants submit that, to the extent one of ordinary skill in the art would find this type of information beneficial, the assays and characterization protocols provided in the Specification could be employed to generate this type of data. For example, potassium channel activity assays, such as those disclosed and/or referenced in the Specification could be employed.

V.C. Specific Epitopes

The Patent Office states the Specification does not disclose any specific epitopes or domains and therefore that the claims are not enabled. Applicants submit it is not necessary to provide this information in order to enable the claims, in view of the direction provided in the Specification. See, for example, page 70 line 30 through page 72, line 30, wherein a discussion of the identification of epitopes is presented, as well as direction regarding the generation and use of an epitope once it is identified by following the direction provided.

V.D. Sequences with at Least 95% Identity to SEQ ID NO:1

The Patent Office additionally rejected the claims because it is the Patent Office's position that the Specification does not teach a nucleic acid sequence with at least 95% identity to the claimed sequence. Applicants again submit that there is no requirement that applicants provide

examples of sequences that are at least 95% identical to SEQ ID NO:1. Applicants have provided SEQ ID NO:1 itself, and direction is provided in the Specification regarding the generation of variant sequences, as discussed above. Applicants also note that guidance is provided in the selection of appropriate algorithms to employ in the identification of sequences that are at least 95% identical to SEQ ID NO:1 (see, e.g., page 56, line 21 through page 58, line 21).

In view of the above, applicants submit that claims 1-4 and 8-9 are in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph. Accordingly, applicants respectfully request that the rejection of claims 1-4 and 8-9 under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn.

VI. Response to the Rejection of Claims 1-4 and 8-9 Under 35 USC 112, First Paragraph, Written Description

The Patent Office rejected claims 1-4 and 8-9 as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. More particularly, the Patent Office contends the disclosure "of one K+betaM3 polynucleotide species (SEQ ID NO:1) and one K+betaM3 polypeptide species (SEQ ID NO:2) is not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all variants, fragments, domains, and epitopes with at least 95% sequence identity to the human K+betaM3 polynucleotide comprising SEQ ID NO:1." Office Action, page 12. Applicants traverse and submit the following comments.

Applicants note that the Guidelines for Examination of Patent Applications Under the 35 USC 112, ¶1 "Written Description" Requirement indicate that the written description requirement can be satisfied by "sufficient description of a representative number of species by actual reduction to practice, reduction to drawings or by disclosure of relevant, identifying characteristics." Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1 "Written Description" Requirement, 66 Fed. Reg. 1099, 1105 (Jan. 5, 2001). See also, University of California v. Eli Lilly, 119 F.3d 1559 (Fed. Cir. 1997) and MPEP §2163.II.A.ii.

Applicants submit that the specification as filed discloses an extensive list of representative species and relevant characteristics of the species, thereby satisfying the written description requirement of 35 U.S.C. §112, first paragraph. Particularly, applicants direct attention to pages 37-

39 of the specification, wherein an extensive list of N-terminal and C-terminal deletion polypeptides are disclosed. The specification states "polynucleotide sequences encoding these polypeptides are also provided" (Specification, page 39, line 35). These deletion polypeptides comprise fragments of the nucleic acid and polypeptide sequences of SEQ ID NO:1. These polynucleotide sequences (a) would be expected to hybridize under stringent conditions (which are described in the specification, including Table 2 presented therein) to the polynucleotides specified in the claims, (b) have a nucleotide sequence that is at least 95% identical to a sequence provided in the claims; and (c) do not encode the polypeptide set forth as SEQ ID NO:1. Therefore, applicants submit that the amino acid and/or polynucleotide sequences are representative of the claimed genus.

Applicants further note that in addition to the disclosed N- and C-terminal deletion polynucleotides, the specification describes the use of conservative substitutions in generating variants of the polynucleotides and polypeptides of the present invention (see, e.g., Table III). Such variants can have a different sequence from that of SEQ ID NO:1, yet retain the properties recited in the claims. Thus, this group of variants highlights yet more species that are representative of the claimed genus.

Next, applicants draw attention to the statement that "[g]enerally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosures necessary to satisfy the written description requirement." Guidelines for Examination of Patent Applications Under the 35 USC 112, ¶1 "Written Description" Requirement, 66 Fed. Reg. 1099, 1105 (Jan. 5, 2001). As noted, applicants submit that the relative level of skill in the pertinent field is very high. Therefore, applicants submit that given the high level of skill in the field identified by the Patent Office, the large number of species representative of the claimed genus disclosed in the present specification, coupled with the discussion of their relevant identifying characteristics, the invention is fully described in accordance with 35 U.S.C. §112, first paragraph.

Applicants submit that, in view of (a) the extensive disclosure of N- and C-terminal deletion polypeptides and the polynucleotides that encode these polypeptides, presented in the specification, (b) the disclosure of species comprising conservative substitutions of SEQ ID NO:1, (c) the recitation of identifying characteristics of the members of the claimed genus, and (d) the high level of skill in the art, claims 1-4, 8, 9 and 16 are in accord with the Written Description Guidelines and the pertinent case law (see, e.g., University of California v. Eli Lilly, 119 F.3d 1559 (Fed. Cir. 1997)), and that the written description requirement of 35 U.S.C. §112, first paragraph, has been met. Summarily, applicants submit that one of ordinary skill in the art would recognize that

Applicants had invented what was claimed, which is the standard against which the adequacy of a written description is gauged. Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555 (Fed. Cir. 1991). Accordingly, applicants respectfully request that the rejection of claims 1-4 and 8-9 under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn.

VII. Response to the Rejection of Claims 1-4, 8-9 and 16-19 Under 35 U.S.C. §112, First Paragraph, Availability of Deposit

The Patent Office rejected claims 1-4, 8-9 and 16-19 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention. Summarily, it is the Patent Office's position that it is not apparent from the Specification that the claimed nucleic acid molecules are available to the public. Applicants submit the following comments.

Applicants submit herewith a statement by an attorney of record over his or her signature and registration number stating that the specific nucleic acid molecules have been deposited under the Budapest Treaty and that the nucleic acid molecules will be irrevocably and without restriction or condition released to the public upon the issuance of a patent. In view of this submission, applicants respectfully request that the rejection of claims 1-4, 8-9 and 16-19 under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn.

VIII. Response to the Rejection of Claims 1-4, 8-9 and 16-19 Under 35 U.S.C. §112, Second Paragraph

The Patent Office rejected claims 1-4, 8-9 and 16-19 under 35 U.S.C. §112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

First, the Patent Office states "[t]he term 'included in ATCC Deposit No:' in claims 1-4, 8-9 and 16-29 is a relative term which renders the claims indefinite. The term 'included in ATCC Deposit No:' is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one or ordinary skill in the art would not reasonably be apprised of the scope of the invention. It is not clear if SEQ ID NO:1 is the cDNA sequence of ATCC Deposit No. XXX or if there is a larger DNA sequence (other than SEQ ID NO:1) encompassed by ATCC Deposit No:XXX." Office Action, page 15.

Applicants have amended claims 1 and 16 to clarify that SEQ ID NO:1 is the cDNA sequence of ATCC Deposit No. PTA-4055.

The Patent Office then states, [t]he term 'polynucleotide which represents the complementary sequence' in claims 1-4, 8-9 and 16-19 is a relative term which renders the claim indefinite (see for example, claim 1(j)). The term 'polynucleotide which represents the complimentary sequence' is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention." Office Action, page 15. The Patent Office suggests, "this issue could be overcome by amending the claims to recite ' a polynucleotide which is the complementary sequence...'." Office Action, page 15.

Although applicants disagree with the Patent Office's position, in an effort to advance prosecution applicants have amended claims 1 and 16 as suggested by the Patent Office.

Next, the Patent Office states "[s]tringency is relative, and the art does not recognize a single set of conditions as stringent. The specification also does not provide an unambiguous definition for the term. In the absence of a recitation of clear hybridization conditions (e.g., "hybridizes at wash conditions consisting of A X SSC and B% SDS at C°C"), claims 1-4 and 8-9 fail to define the metes and bounds of the varying structures of polynucleotides recited in the claimed methods." Office Action, page 15-16.

Applicants direct attention to page 47-48, on which Table 2 appears, and to page 49, line 5 through page 50, line 28, on which a description of Table 2 is provided. Table 2 discloses various examples of stringent hybridization conditions, which are supplemented by the discussion on pages 46-50. Applicants submit, therefore, that a recitation of hybridization conditions is presented in the Specification.

In view of the amendments to the claims and the remarks presented above, applicants submit that claims 1-4, 8-9 and 16-19 are in compliance with 35 U.S.C. §112, second paragraph. Accordingly, applicants request that the rejection of these claims under 35 U.S.C. §112, second paragraph, be withdrawn. Applicants further submit claims 1-4, 8-9 and 16-19 are in condition for allowance and respectfully solicit the same.

VI. Conclusions

In light of the above amendments and remarks, applicants respectfully request that the rejections of record be withdrawn. Applicants further submit that the subject patent application is in condition for allowance and courteously solicit a Notice of Allowance.

If any small matter should remain outstanding after the Patent Office has had an opportunity to review the instant paper, the Patent Office is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Office Action.

Although it is believed no additional fee is due, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment associated with the filing of this correspondence to Deposit Account Number 19-3880. Furthermore, if any extension of time not already accounted for is required, such extension is hereby petitioned for, and it is requested that any fee due for said extension be charged to Deposit Account Number 19-3880.

Respectfully submitted,

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